102. (New) The method of claim 82, wherein the glycoprotein comprises an immunoglobulin.--

REMARKS

Claims 12-20, 23-31, 44-53, and 55-102 are pending with entry of this amendment. Claims 12, 23, 44, 57 and 82 have been amended. Claims 98-102 are newly added. No new matter has been introduced with the foregoing amendment and newly added claims. Early action on the merits is respectfully requested.

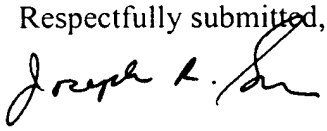
Attached hereto is a marked-up version of the changes made to the specification and claims by the current amendment. The attached page is captioned "Version with markings to show changes made." The amendments to the specification herein make the same changes to the specification set forth in the November 9, 2001 Preliminary Amendment, but in "marked-up version" format.

The amendments to claims 12, 23, 44, 57 and 82 have been made to more particularly point out and distinctly claim that which Applicants regard as their invention. Support for the amendments to the claims can be found throughout the specification as originally filed. More particularly, support is found, for example, at page 9, line 23-25. Support for new claims 98-102 can be found, for example, at page 8, lines 20-22.

As such, Applicants respectfully request that the amendments and new claims be entered. Early examination on the merits is respectfully requested.

If the Examiner believes a telephone conference would expedite prosecution of this application, please telephone the undersigned at 925-472-5000.

Respectfully submitted,



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VERSION WITH MARKINGS TO SHOW CHANGES MADE

In the Specification:

Please rewrite the first paragraph on page 1 as follows:

This application is a divisional of U.S. Patent Application No. 09/007,741, filed January 15, 1998, now U.S. Patent No. 6,399,336, **[This]** which application claims priority to US Provisional Application 60/035,710, filed January 16, 1997, which are incorporated herein by reference in their **[its]** entirety for all purposes.

Please rewrite the paragraph at page 2, line 3 as follows:

Production of glycoproteins in transgenic animals has some of the same problems as mammalian cell culture. While the "production" of a glycoprotein is inherently better controlled, it is also less susceptible to manipulation. If glycosylation is not complete, there is little that can be done with the animals to alter the outcome. With transgenic animals there is often another problem. While the predominant sialic acid in humans is N-acetyl-neuraminic acid (NeuAc), goats, sheep and cows all produce a large fraction of their total sialic acid as N-glycolyl-neuraminic acid (NeuGc). Although the impact of this modification is not yet fully explored from a functional or regulatory perspective, it is known that the NeuGc substitution is antigenic in humans (Varki (1992) *Glycobiology* **2:** 25-40).

Please rewrite the paragraph at page 3, line 5 as follows:

Sialyltransferases that are useful in the methods of the invention typically have a sialyl motif that comprises about 48-50 amino acids, within which about 40% of the amino acids are identical to the consensus sequence RCAVVSSAG---DVGSKT (where --- indicates a variable number of amino acid residues such that the motif is about 48-50 residues in length). Examples of sialyltransferases that are suitable for use in the

present invention include ST3Gal III (preferably a rat ST3Gal III), ST3Gal IV, ST3Gal I, ST6Gal I, ST3Gal V, ST6Gal II, ST6GalNAc I, ST6GalNAc II, and ST6GalNAc III (the sialyltransferase **[nomemclature]** nomenclature used herein is as described in Tsuji *et al.* (1996) *Glycobiology* 6: v-xiv). The methods of the invention can involve sialylation of recombinant glycoproteins with more than one sialyltransferase; for example, with an ST3Gal III and an ST3Gal I, or an ST3 Gal III and an ST6 GalI, or other combinations of enzymes. The sialic acid donor moiety used in the claimed methods is generally CMP-sialic acid, which can be added to the reaction directly or can be enzymatically generated *in situ*. The sialic acids used in a preferred embodiment are selected from the group consisting of NeuAc and NeuGc.

Please rewrite the paragraph at page 3, line 5 as follows:

Ara	= arabinosyl;
Fru	= fructosyl;
Fuc	= fucosyl;
Gal	= galactosyl;
GalNAc	= **[N-acetylgalacto]** N-acetylgalactosaminyl;
Glc	= glucosyl;
GlcNAc	= **[N-acetylgluco]** N-acetylglucosaminyl;
Man	= mannosyl; and
NeuAc	= sialyl (typically N-acetylneuraminyl).

12. (Amended) A commercial-scale method of sialylating a saccharide group on a recombinant glycoprotein, the method comprising contacting a saccharide group which comprises a galactose or N-acetylgalactosamine acceptor moiety on a recombinant glycoprotein with a sialic acid donor moiety **[The method of claim 1]**, wherein the sialyltransferase is a recombinant bacterial sialyltransferase ,in a reaction

mixture which provides reactants required for sialyltransferase activity for a sufficient time and under appropriate conditions to transfer sialic acid from said sialic acid donor moiety to said saccharide group.

23. (Amended) A commercial-scale method of sialylating a saccharide group on a recombinant glycoprotein, the method comprising contacting a saccharide group which comprises a galactose or an N-acetylgalactosamine acceptor moiety on a recombinant glycoprotein with a sialic acid donor moiety and a bacterial sialyltransferase in a reaction mixture which provides reactants required for sialyltransferase activity for a sufficient time and under appropriate conditions to transfer sialic acid from said sialic acid donor moiety to said saccharide group.

44. (Amended) A commercial-scale method for *in vitro* sialylation of saccharide groups present on a glycoprotein, said method comprising contacting said saccharide groups with a sialyltransferase, **[The method of claim 32,]** wherein the sialyltransferase is a bacterial sialyltransferase , a sialic acid donor moiety, and other reactants required for sialyltransferase activity for a sufficient time and under appropriate conditions to transfer sialic acid from said sialic acid donor moiety to said saccharide group.

57. (Amended) A commercial-scale method for *in vitro* sialylation of terminal galactose residues **[present]** on a glycoprotein, said method comprising contacting said glycoprotein with a reaction mixture that comprises a sialyltransferase, a sialic acid donor moiety, and other reactants required for sialyltransferase activity, for a sufficient time and under appropriate conditions to transfer sialic acid from said sialic acid donor moiety to said terminal galactose residues **[, wherein said ST3Gal III sialyltransferase is present at a concentration of less than about 50 mU per mg of glycoprotein]**.

82. (Amended) A commercial-scale method for altering the glycosylation pattern of a glycoprotein *in vitro*, the method comprising contacting a glycoprotein-linked saccharide with a galactosyltransferase in the presence of UDP-galactose under suitable conditions for the galactosyltransferase to transfer a galactose residue from the UDP-galactose to the saccharide to form a galactosylated saccharide.

Please add the following new claims 98-102:

98. (New) The method of claim 12, wherein the glycoprotein comprises an immunoglobulin.

99. (New) The method of claim 23, wherein the glycoprotein comprises an immunoglobulin.

100. (New) The method of claim 44, wherein the glycoprotein comprises an immunoglobulin.

101. (New) The method of claim 57, wherein the glycoprotein comprises an immunoglobulin.

102. (New) The method of claim 82, wherein the glycoprotein comprises an immunoglobulin.